



GAU 1631

PATENT
Attorney Docket No. 11034US02 / 100-248.P1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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JAN 16 2001

In the Application of:

Beamer, et al.

Application No.: 09/446,415

371 Date: July 19, 2000

U.S. National Phase of: PCT/US98/13007

International Filing Date: June 22, 1998

For: BACTERICIDAL/PERMEABILITY-
INCREASING PROTEIN:
CRYSTALLIZATION, X-RAY
DIFFRACTION, THREE-
DIMENSIONAL STRUCTURE
DETERMINATION, RATIONAL
DRUG DESIGN AND MOLECULAR
MODELING OF RELATED
PROTEINS

Examiner: A. Marschel, Ph.D.

Group Art Unit: 1631

CERTIFICATE OF MAILING

I hereby certify that this
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mail, postage prepaid, under 37 C.F.R.
§1.8, in an envelope addressed to:
Commissioner for Patents, Washington,
D.C. 20231 on January 8, 2001.

Janet M. McNicholas

Janet M. McNicholas, Ph.D.
Registration No. 32,918

TRANSMITTAL LETTER

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Transmitted herewith for appropriate action are the following:

1. A Response to the Office Action dated December 12, 2000 with Election;
2. One return postcard.

The Commissioner is hereby authorized to charge any additional fees which may be required to Deposit Account No. 13-0017 in the name of McAndrews, Held & Malloy, Ltd.

Respectfully submitted,

Dated: January 8, 2001



Janet M. McNicholas, Ph.D.

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(312) 775-8000



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Janet M. McNicholas

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Registration No. 32,918

RESPONSE TO OFFICE ACTION OF DECEMBER 12, 2000 WITH ELECTION

Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the Office Action dated December 12, 2000 in the above-
identified application requiring an election of species. No fee is due with this timely filed
response, however, the Commissioner is hereby authorized to charge Account no. 13-0017

(McAndrews, Held & Malloy) for any fee deficiency, or credit any overpayment associated with this application.


ELECTION OF SPECIES

In response to the Office Action of December 12, 2000, requiring an election of species, Applicants elect Specie A stated by the Examiner to be: "Methods of Modeling a BPI protein (Claims 1-6 and 15-23)." A copy of Claims 1-6 and 15-23 are attached for the Examiner's convenience as Appendix A.

In view of the foregoing election, Applicants submit that a complete response has been made to the election requirement and request examination of the elected claims. The Examiner is invited to telephone Applicants' undersigned representative if the Examiner believes, for any reason, that personal communication would expedite prosecution of this application.

Respectfully submitted,

Dated: January 8, 2001


Janet M. McNicholas, Ph.D.
Registration No. 32,918

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(312) 775-8000

Appendix A
Specie A Claims 1-6 and 15-23
of U.S. Application No. 09/446,415

1. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, or fragment, analog or variant thereof, to model a BPI protein.
2. Use of atomic coordinates of bactericidal/permeability-increasing ("BPI") protein, or fragment, analog or variant thereof, to model a BPI-related lipid transfer protein.
3. The use according to claim 2, wherein the BPI-related lipid transfer protein is lipopolysaccharide-binding protein (LBP), cholesteryl ester transferase protein (CETP) or phospholipid transfer protein (PLTP), or fragment, analog or variant thereof.
4. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 31.
5. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.
6. The use according to any of claims 1-3, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3 and a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.
15. The use according to any of claims 1 - 14, wherein said atomic coordinates are according to Table 4.
16. A method of three-dimensional modeling of a bactericidal/permeability-increasing ("BPI") protein comprising the steps of:
 - (a) providing three-dimensional atomic coordinates derived from X-ray diffraction measurements of a BPI protein in a computer readable format;

- (b) inputting the data from step (a) into a computer with appropriate software programs;
 - (c) generating a three-dimensional structural representation of the BPI protein suitable for visualization and further computational manipulation.
17. A method of three-dimensional modeling of a bactericidal/permeability-increasing ("BPI")-related lipid transfer protein comprising the steps of:
- (a) providing three-dimensional atomic coordinates derived from X-ray diffraction measurements of a BPI protein in a computer readable format;
 - (b) inputting the data from step (a) into a computer with appropriate software programs;
 - (c) generating a three-dimensional structural representation of the BPI-related lipid transfer protein suitable for visualization and further computational manipulation.
18. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3.
19. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.
20. The use according to any of claims 16-17, wherein the BPI protein comprises a binding site characterized by amino acid residues of at least one binding pocket as defined in Table 3 and a binding site characterized by at least one amino acid sequence, or variant of the sequence, selected from positions about 17 to about 45, positions about 36 to about 54, positions about 65 to about 99, positions about 84 to about 109, positions about 142 to about 164, or positions about 142 to about 169 of BPI.
21. A method for providing an atomic model of a BPI protein, or fragment, analog or variant thereof, comprising
- (a) providing a computer readable medium having stored thereon atomic coordinate/x-ray diffraction data of the BPI protein, or fragment, analog or variant thereof, in crystalline form, the data sufficient to model the

- three-dimensional structure of the BPI protein, or fragment, analog or variant thereof;
- (b) analyzing, on a computer using at least one subroutine executed in said computer, atomic coordinate/x-ray diffraction data from (a) to provide atomic coordinate data output defining an atomic model of said BPI protein, or fragment, analog or variant thereof, said analyzing utilizing at least one computing algorithm selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron map visualization, model building, rigid body refinement, positional refinement; and
 - (c) obtaining atomic coordinate data defining the three-dimensional structure of at least one of said BPI protein, or fragment, analog or variant thereof.

22. A method according to claim 21, wherein said computer readable medium further has stored thereon data corresponding to a nucleic acid sequence or an amino acid sequence data comprising at least one structural domain or functional domain of a BPI, LBP, CETP or PLTP corresponding to at least one BPI or mutant primary sequence of Figures 2-20 or Table 2, or a fragment thereof; and wherein said analyzing step further comprises analyzing said sequence data.

23. A computer-based system for providing atomic model data of the three-dimensional structure of BPI protein, or fragment, analog or variant thereof, a BPI mutant or a BPI fragment, comprising the following elements:

- (a) at least one computer readable medium (CRM) having stored thereon atomic coordinate/x-ray diffraction data of said BPI protein, or fragment, analog or variant thereof;
- (b) at least one computing subroutine that, when executed in a computer, causes the computer to analyze atomic coordinate/x-ray diffraction data from (a) to provide atomic coordinate data output defining an atomic model of said BPI protein, or fragment, analog or variant thereof, said analyzing utilizing at least one computing subroutine selected from the group consisting of data processing and reduction, auto-indexing, intensity scaling, intensity merging, amplitude conversion, truncation, molecular replacement, molecular alignment, molecular refinement, electron density map calculation, electron density modification, electron

map visualization, model building, rigid body refinement, positional refinement; and

- (c) retrieval means for obtaining atomic coordinate output data substantially defining the three-dimensional structure of said BPI protein, or fragment, analog or variant thereof.